Corrected Amendment to the Specification:

Please amend the Specification as follows. In the description of amendments to the Specification, below, underlining is used to indicate added text; while, ~~strikeout~~ is used to indicate deleted text.

Please replace the paragraph beginning on page 4, line 14 with the following amended paragraph:

Another object of the invention is a purified or isolated nucleic acid having at least 90%, preferably 95%, more preferably 98% and most preferably 99% nucleotide identify with the nucleotide sequence of SEQ ID ~~N°1~~NO:1, or a sequence complementary thereto.

Please replace the paragraph beginning on page 4, line 18 with the following amended paragraph:

A further object of the present invention is a purified or isolated nucleic acid encoding a polypeptide having at least 80%, preferably 90%, more preferably 95%, and most preferably 98 or 99% amino-acid identity with the porcine polypeptide of the amino-acid sequence of SEQ ID ~~N°~~NO:5 or with a peptide fragment thereof, or a sequence complementary thereto.

Please replace the paragraph beginning on page 4, line 23 with the following amended paragraph:

Polypeptides having amino-acid identity with the $\alpha_2\delta$-1 subunit of the invention encompass polypeptides:

-that have primary structures which are related to the $\alpha_2\delta$-1 subunit of any one of the amino-acid sequences of SEQ ID ~~N°~~NO:5, due to the high sequence identity between the amino-acid sequences; or

-that are biologically related to the polypeptides of any one of the amino-acid sequences of SEQ ID ~~N°~~NO:5, either because these homologous polypeptides are recognized by antibodies

specifically directed against the amino-acid sequence of SEQ ID ~~N°~~NO:5 and/or because these homologous polypeptides have the same biological activity as the polypeptides of the amino-acid sequence of SEQ ID ~~N°~~NO:5, such as for example the capacity of binding [^{3}H]gabapentin with suitable affinity.

Please replace the paragraph beginning on page 5, line 1 with the following amended paragraph:

It is important to note that the first 24 amino acids of the amino acid sequence of SEQ ID ~~N°~~NO:5 is a signal peptide. This signal peptide can in some embodiments be deleted or replaced by a signal peptide from another species. For example, if one wishes to express this protein in insect cells, the native porcine $\alpha_2\delta$-1 signal peptide can be replaced by a signal peptide of insect origin.

Please replace the paragraph beginning on page 7, line 16 with the following amended paragraph:

In order to determine the minimum fragment of the δ subunit required for [^{3}H]gabapentin binding, the inventors constructed mutants with C-terminal deletions of the δ component. C-terminally truncated mutants extending to residues 966 and 983 of SEQ ID ~~N°~~NO:5 both do not bind [^{3}H]gabapentin. However, mutants extending to residues 1018, 1036, 1063 and 1084 of SEQ ID ~~N°~~NO:5 exhibit gabapentin binding activity. Thus, the inventors have identified a 35-residue stretch between residues 984 to 1018 of SEQ ID ~~N°~~NO:5 which, when delected with the C-terminal residues which follow, results in the loss of specific [^{3}H]gabapentin binding.

Please replace the paragraph beginning on page 8, line 4 with the following amended paragraph:

In order to determine the optimal deletions on the $\alpha_2\delta$-1 subunit cDNA that yield a soluble secreted protein devoid of membrane anchorage structures, the inventors tested the expression of

several porcine $\alpha_2\delta$-1 subunit cDNA deletion mutants. The inventors found that by deleting from the porcine $\alpha_2\delta$-1 subunit cDNA a nucleotide sequence encoding as much as amino-acids 967 to 1091 of the native protein, soluble secreted polypeptides could be obtained. On the other hand, the minimal deletion required to achieve solubility appears to be located around nucleotides encoding amino-acids 1064 to 1091 of the sequence of SEQ ID ~~N°~~NO:5. In this regard, the mutant polypeptide expressed using a cDNA deletion mutant from which a sequence encoding amino-acids 1064 to 1091 is removed is found in both soluble and membrane-associated forms, with [^{3}H]gabapentin binding properties similar to that of the wild type protein. Furthermore, a mutant protein expressed using a cDNA deletion mutant from which a nucleotide sequence encoding amino-acids 1085 to 1091 is removed recovers its membrane anchorage properties. Also, mutant proteins expressed using cDNA deletion mutants from which nucleotide sequences encoding either amino-acids 1037 to 1091 or amino-acids 1019 to 1091 of SEQ ID ~~N°~~NO:5 are removed are found in soluble form.

Please replace the paragraph beginning on page 8, line 20 with the following amended paragraph:

The inventors believe that the soluble secreted $\alpha_2\delta$-1 subunit polypeptides which are as close as possible to the native sequence and which are therefore more likely to retain their native folding and hence thir [^{3}H]gabapentin binding properties are those corresponding to the native protein in which amino-acid stretch 985-1091 to 1079-1091 of the amino-acid sequence of SEQ ID ~~N°~~NO:5 has been deleted. The skilled scientist can quite easily determine within this 90 amino-acid stretch the optimal $\alpha_2\delta$-1 subunit polypeptides.

Please replace the paragraph beginning on page 8, line 27, with the following amended paragraph:

The invention therefore particularly concerns a nucleotide sequence encoding a polypeptide having at least 80% identity with the polypeptide comprising from amino-acid 1 to between

amino-acids 985 and 1054, preferably between amino-acids 985 and 1059, and most preferably between amino-acids 1019 and 1064 of SEQ ID ~~N°~~NO:5 or SEQ ID ~~n°~~NO:14.
Preferred nucleotide sequences include those of SEQ ID ~~N°~~NO:2, SEQ ID ~~N°~~NO:3, SEQ ID ~~N°~~NO:4, SEQ ~~ID n°~~ID NO:19, SEQ ID ~~n°~~NO:20 and SEQ ID ~~n°~~NO:21.

Please replace the paragraph beginning on page 9, line 2 with the following amended paragraph:

The present invention also concerns a purified or isolated polynucleotide comprising at least 10 consecutive nucleotides of a nucleic acid encoding the porcine $\alpha_2\delta$-1 subunit described herein, preferably at least 10 consecutive nucleotides of the nucleotide sequence of SEQ ID ~~N°~~NO:1, or a sequence complementary thereto.

Please replace the paragraph beginning on page 9, line 9 with the following amended paragraph:

These nucleic acids are useful as probes in order to detect the presence of at least a copy of a nucleotide sequence encoding the porcine $\alpha_2\delta$-1 subunit, more particularly the presence of at least a copy of a nucleotide sequence of SEQ ID ~~N°~~NO:1 or a sequence complementary thereto or a fragment or a variant thereof in a sample. The sequence of such nucleic acids could be slightly modified (for example by substituting one nucleotide for another) without substantially affecting the ability of such modified sequence to hybridize with the targeted sequence of interest.

Please replace the paragraph beginning on page 11, line 23 with the following amended paragraph:

In a first preferred embodiment of the above method, the nucleic acid encodes a porcine $\alpha_2\delta$-1 subunit of SEQ ID ~~N°~~NO:5, or a secreted soluble $\alpha_2\delta$-1 subunit polypeptide of SEQ ID ~~n°~~NO:6, SEQ ID ~~n°~~NO:7, SEQ ID ~~n°~~NO:8, SEQ ID ~~n°~~NO:15, SEQ ID ~~n°~~NO:16 and SEQ ID ~~n°~~NO:17.

Please replace the paragraph beginning on page 11, line 26 with the following amended paragraph:

In a second preferred embodiment of the above method, a first primer is the nucleotide sequence of SEQ ID ~~N°~~NO:9 and a second primer is complementary to a portion of the 3' untranslated region of SEQ ID ~~N°~~NO:5, such as the primer having the sequence of SEQ ID ~~N°~~NO:22.

Please replace the paragraph beginning on page 12, line 7, with the following amended paragraph:

In a first preferred embodiment of the kit described above, the nucleic acid encodes the porcine $\alpha_2\delta$-1 subunit of SEQ ID ~~N°~~NO:5.

Please replace the paragraph beginning on page 12, line 12 with the following amended paragraph:

In a third embodiment of the above amplification kit, the amplification primers are respectively the nucleotide sequences of SEQ ID ~~N°~~NO:9 and SEQ ID ~~N°~~10.

Please replace the paragraph beginning on page 12, line 18 with the following amended paragraph:

The present invention also encompasses a family of recombinant vectors comprising any one of the nucleic acids described herein. Firstly, the invention deals with a recombinant vector comprising a nucleic acid selected from the group consisting of:

(a) a purified or isolated nucleic acid encoding a porcine $\alpha_2\delta$-1 subunit, and more preferably a polypeptide having at least 80% amino acid identity with the polypeptide of SEQ ID ~~N°~~NO:5, or a sequence complementary thereto;

(b) a purified or isolated nucleic acid having at least 90% nucleotide identity with a polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID ~~N°~~NO:2, SEQ ID ~~N°~~NO:3, SEQ ID ~~N°~~NO:4, SEQ ID ~~n°~~NO:19, SEQ ID ~~n°~~NO:20 and SEQ ID ~~n°~~NO:21 or a sequence complementary thereto;

(c) a purified or isolated polynucleotide comprising at least 10 consecutive nucleotides of a nucleic acid described in (a) or a sequence complementary thereto.

Please replace the paragraph beginning on page 13, line 5, with the following amended paragraph:

These include, but are not restricted to, nucleic acids encoding from amino-acid 1 to between amino-acids 985 to 1054, preferably between amino-acids 984 and 1059, more preferably between amino-acids 1019 to 1064, SEQ ID ~~N°~~NO:5 and SEQ ID ~~N°~~NO:14.

Please replace the paragraph beginning on page 13, line 8 with the following amended paragraph:

Another preferred embodiment of the recombinant vectors according to the invention consist of expression vectors comprising a nucleic acid encoding an $\alpha_2\delta$-1 subunit polypeptide of the invention, and more preferably a nucleic acid encoding a polypeptide selected from the group consisting of the amino acid sequences of SEQ ID ~~N°~~NO:5, SEQ ID ~~N°~~NO:6, SEQ ID ~~N°~~NO:7, SEQ ID ~~N°~~NO:8, SEQ ID ~~n°~~NO:15, SEQ ID ~~n°~~NO:16 and SEQ ID ~~n°~~NO:17.

Please delete the following paragraph, beginning on page 15, line 14, as shown below:

~~Preferred eukaryotic promoters are the (to be completed by inventors)~~

Please replace the paragraph beginning on page 16, line 2 with the following amended paragraph:

The present invention also concerns a method for producing one of the amino acid sequences described herein and especially a polypeptide selected from the group consisting the amino acid sequences of SEQ ID ~~N°~~NO:5, SEQ ID ~~N°~~NO:6, SEQ ID ~~N°~~NO:7, SEQ ID ~~N°~~NO:8, SEQ ID ~~n°~~NO:15, SEQ ID ~~n°~~NO:16 or SEQ ID ~~n°~~NO:17 wherein said method comprises the steps of:

(a) inserting the nucleic acid encoding the desired amino acid sequence in an appropriate vector;

(b) culturing, in an appropriate culture medium, a host cell previously transformed or transfected with the recombinant vector of step (a);

(c) harvesting the culture medium thus obtained or lyse the host cell, for example by sonication or osmotic shock;

(d) separating or purifying, from said culture medium, or from the pellet of the resultant host cell lysate, the thus produced recombinant polypeptide of interest.

Please replace the paragraph beginning on page 17, line 12, with the following amended paragraph:

In a further preferred embodiment, the polypeptide comprises an amino acid sequence having at least 80%, preferably 90%, more preferably 95%, and most preferably 98% or 99% amino acid identity with the amino acid sequence of SEQ ID ~~N°~~NO:5, SEQ ID ~~n°~~NO:6, SEQ ID ~~N°~~NO:7, SEQ ID ~~N°~~NO:8, SEQ ID ~~N°~~NO:15, SEQ ID ~~N°~~NO:16 and SEQ ID ~~N°~~NO:17.

Please replace the paragraph beginning on page 17, line 19, with the following amended paragraph:

The invention also relates to a porcine $\alpha_2\delta$-1 subunit, or a secreted soluble $\alpha_2\delta$-1 subunit polypeptide comprising amino acid changes ranging from 1, 2, 3, 4, 5, 10, 20, 25, 30, 35, 40 substitutions, additions or deletions of one amino acid as regards to polypeptides of anyone of

the amino acid sequences of the present invention. Preferred sequences are those of SEQ ID ~~N°~~NO:5, SEQ ID ~~N°~~NO:6, SEQ ID ~~N°~~NO:7, SEQ ID ~~N°~~NO:8, SEQ ID ~~n°~~NO:15, SEQ ID ~~n°~~NO:16 and SEQ ID ~~n°~~NO:17.

Please replace the paragraph beginning on page 20, line 16 with the following amended paragraph:

Primers were designed to amplify the missing 5' portion of the $\alpha_2\delta$ cDNA by 5' Rapid Amplification of cDNA Ends (5' RACE). A series of primers were synthesized based on the $\alpha_2\delta$ cDNA antisense sequence derived from the $\alpha_2\delta$ coding region obtained above, all are downstream (3') of a unique *Bgl* I restriction site. Total RNA was prepared from porcine cortical membranes and single strand cDNA synthesized using SuperScript II reverse transcriptase and the primer furthest from the Bgl I site (JB039; 5'-TTCTCTAATTCTGCATCAAGG-3', SEQ ID ~~N°~~NO:24). The cDNA was then purified and tailed with dCTP's using terminal deoxynucleotidyl transferase. Aliquots of this tailing reaction were then PCR amplified through 35 cycles using *Taq* DNA polymerase and the primer pair JB041 (5'-TTTGGATGTAATAAAACATAG-3', SEQ ID ~~N°~~NO:25) and the universal amplification primer (5'-CUACUACUACUAGGCCACGCGTCGACTAGTAC-3', SEQ ID ~~N°~~NO:26). Several PCR products were generated and Qiaex gel-purified. All products were positive by Southern blot hybridization using a 1,264bp probe (5' $\alpha_2\delta$ coding sequence) derived from a *Hind* III/*Bgl* I restriction digest of pcDNA3-Rab-$\alpha_2\delta$-(+). Each PCR product was sub-cloned into pBluescript. The 5' and 3' ends of each insert were sequenced confirming that all clones contain $\alpha_2\delta$ sequence as predicted from the Southern blot experiment. The longest of the inserts contained sequence that extended 24bp into the non-coding sequence of the $\alpha_2\delta$ cDNA.

Please replace the paragraph beginning on page 21, line 1 with the following amended paragraph:

The sequence derived from the 5' RACE product was used to design a primer (JB042, 5'-GGGGATTGATCTTCGATCGCG-3'; SEQ ID ~~N°~~NO:9) specific for the 5'-untranslated end of

the cDNA. PCR was then performed with *Pfu* DNA polymerase using JB042 and a primer downstream of the *BglI* site (5'-GCAGATTTGGTTTTAGAAGGG-3', SEQ ID NO:22) The PCR product was ligated to EcoRI linkers (5'-GGAATTCC-3') and then digested with EcoRI and *BglI*. The 1,564-bp fragment (5' portion of the $\alpha_2\delta$ cDNA) was gel-purified.

Please replace the paragraph beginning on page 21, line 32 with the following amended paragraph:

Anti-δ antibodies were raised by immunizing rabbits with a keyhole lympet hemocyanin-conjugated peptide, VEMEDDDFTASLSKQSC (SEQ ID ~~NO~~NO:11), corresponding to the start sequence of the δ polypeptide (residues 922-938, relative to the first residue of the mature α_2 polypeptide). Peptide synthesis and immunization protocols were performed by Genosys Biotechnologies Inc. (The Woodlands, TX)~~,~~

Please replace the paragraph beginning on page 22, line 18 with the following amended paragraph:

~~*For mutants*~~ For mutants C (▲275-1091 (i.e. residues 275 to 1091 deleted)), D (▲ 470-1091), E (▲621-1091), F (▲804-1091), G (▲946-1091), H (▲967-1091), I (▲984-1091), J (▲1019-1091, SEQ ID ~~NO~~NO:6), K (▲1037-1091, SEQ ID ~~NO~~NO:7), L (▲1064-1091, SEQ ID ~~NO~~NO:8), M (▲ 1085-1091), and PCR-WT (3'-untranslated region deleted) amplifications were performed with an anchored 5' primer (JB055, 5'-TGGCTTATCGAAATTAATACG-3', SEQ ID ~~NO~~NO:12), which anneals at position 849-869 in pcDNA3-PC-$\alpha_2\delta$-(+).

Please replace the paragraph beginning on page 22, line 25 with the following amended paragraph:

For mutants A (▲135-1091) and B (▲253-1091), the anchored 5' primer was 5'-AACTCCGGGGATTGATCTTCG-3' (JB115, SEQ ID ~~NO~~NO:13), which anneals at position

971-991. The 3' primer was designed to anneal internally to the $\alpha_2\delta$ coding sequence to generate the specified C-terminally truncated $\alpha_2\delta$ mutant.

Applicants respectfully request entry of the amendments to the Specification set forth above, in order to correct defects in the amendments introduced by Applicants on July 23, 2003. Applicants respectfully submit that the present application will be in condition for allowance, after entry of the present amendments. Office officials, including the Examiner, are invited to contact the undersigned at the telephone number given below, to discuss the amendments, above, or accompanying Petition for Withdrawal or RCE.

Dated: March 4, 2005

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